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Primary Small Cell Neuroendocrine Carcinoma of the Larynx: A Case Report

Ikram Zaytoune[1*], Basma Mahrouch[1], Nassima Kadri[1], Anis Agouzzal[1], Malak Bennani[1], Imane Boujguenna[2], Hanane Rais[2], Mouna Darfaoui[1], Abdelhamid El Omrani[1], Mouna Khouchani[1]

[1]Radiation Oncology Department, Mohammed VI University Hospital, Marrakesh, Morocco
[2]Pathological Anatomy Department, Mohammed VI University Hospital, Marrakesh, Morocco

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***Corresponding author:** Ikram Zaytoune
Radiation Oncology Department, Mohammed VI University Hospital, Marrakesh, Morocco

Abstract | **Case Report**

Small cell neuroendocrine carcinoma of the larynx is a rare entity. The prognosis of this type of tumor is very poor, and the clinical course is rapidly fatal. We report a case of a 62-year-old patient who presented with a two years history of chronic dysphonia. Laryngoscopy revealed a bulging lesion in the glottic and supraglottic region. Morphological and immunohistochemical studies revealed a small cell neuroendocrine tumor. This patient received chemotherapy associated with concomitant radiotherapy with a good clinical and radiological evolution.

Keywords: tumor, Small cell neuroendocrine carcinoma, chronic dysphonia.

INTRODUCTION

Neuroendocrine tumors are rare and can affect several organs, especially the gastrointestinal tract and lungs. The larynx is considered as the most common site in the head and neck, and accounts for less than 0,6% [1]. Laryngeal neuroendocrine carcinomas (NEC) are divided into well-, moderate- and poorly-differentiated neuroendocrine carcinoma. The latter is divided into small cell NEC (SCNEC) and large cell NEC (LCNEC) according to the 4th Edition of the World Health Organization (WHO) Classification of Head and Neck Tumors [2]. They were first described in 1955 by Blanchard and Saunders [3], but the first case of small cell poorly differentiated carcinoma of the larynx, was reported only in 1972 by Van Nostrand and Olofsson [4]. The clinical presentation of poorly differentiated NECs of the larynx is characterized by non-specific symptoms, early and fast progression of the disease, usually with systemic dissemination, and short survival time [5].

Here, we report a case of laryngeal SCNEC who was successfully treated with a combination of chemotherapy and radiotherapy.

CASE REPORT

We report a case of a 62-year-old male, presented to our department with a 2 years history of permanent dysphonia progressively worsening. In fact, there was no dysphagia or dyspnea, nor notion of deterioration of the general state or paraneoplastic syndrome. Anamnesis revealed a consumption of three units of alcohol per week and tobacco smoking history of 30 pack-years. Physical examination showed multiple palpable cervical lymph nodes, matted together creating a hard, fixed 11cm right cervical mass with an unclear boundary, and a 2cm tender left level III cervical mass. A laryngoscopy showed a growth involving the anterior part of both true and false vocal cords, the anterior commissure and the epiglottis.

CT imaging revealed a 2cm lesion of the vocal cords associated to a lysis of the thyroid cartilage, infiltrating the paralaryngeal space with multiple bilateral enlarged cervical lymph nodes (Figure 1).

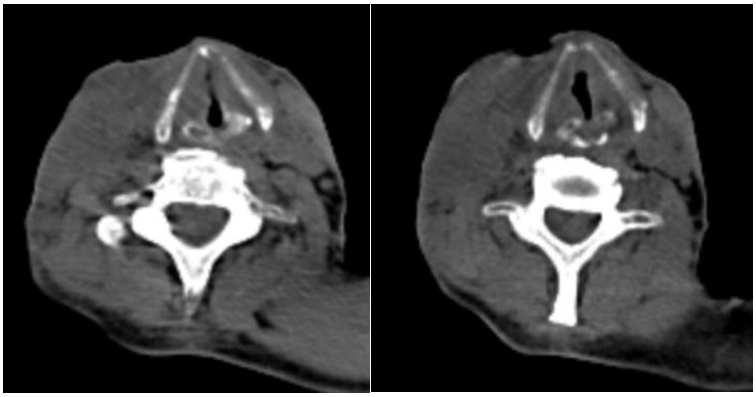

Figure 1: CT Scan showing a lesion of the vocal cords involving the paralaryngeal space with bilateral cervical lymph nodes more pronounced on the right side

Biopsy sample was obtained via suspension laryngoscopy under general anesthesia, and was suggestive of a small cells neuroendocrine carcinoma (Figure 2).

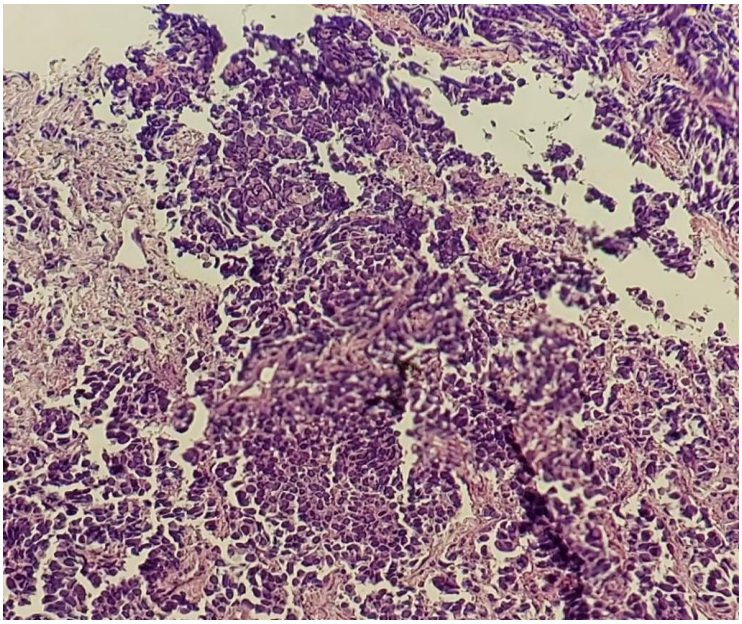

Figure 2: Small cell carcinoma proliferation HE x20

Immunohistochemistry (IHC) showed positivity for CK, CD56, synaptophysin and chromatogranin in tumor cells and negative p53 and p63 (Figure 3).

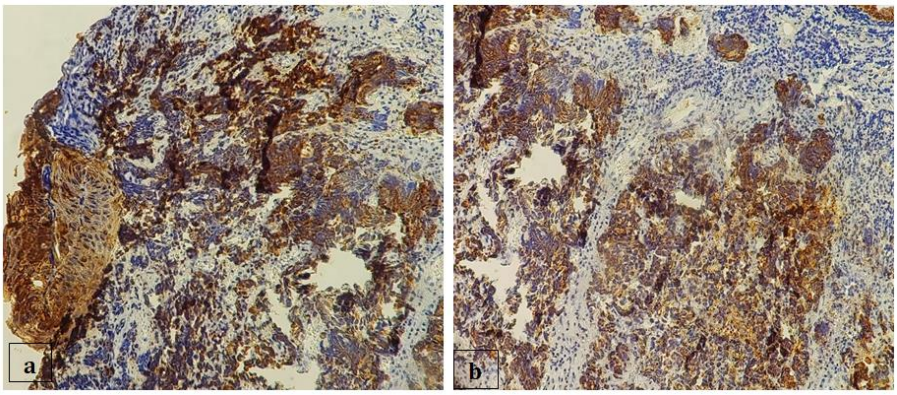

Figure 3 (a, b): Moderate and diffuse cytoplasmic expression of Synaptophysin (a) and Chromogranin (b) in tumor cells

Whole-body OctreoScan was indicative of primary glottic malignancy involving paralaryngeal space with right cervical nodal metastases.

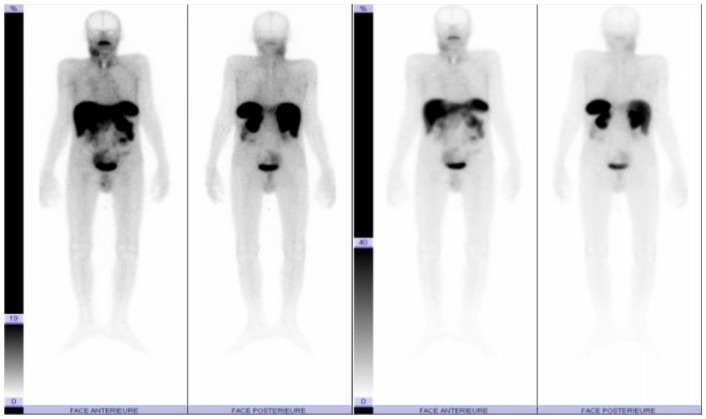

Figure 3: OctreoScan showing a right high cervical hyperfixation on a large secondary lymph node mass without any secondary lung, liver or bone hyperfixation

The patient was staged as cT4N3M0. The case was discussed in the multidisciplinary tumor board and the decision was to offer him neoadjuvant chemotherapy with cisplatin and etoposide for four cycles followed by concomitant chemoradiation with a total dose of 70 Grays (Gy) in 35 fractions of 2Gy. He has completed the treatment with an improvement of his general condition and remained asymptomatic with no evidence of local or regional recurrence during the follow up.

DISCUSSION

Primary SCNEC of the larynx is a rare entity, representing less than 0.5% of all laryngeal carcinomas [6]. It has a very poor prognosis with a five-year survival rate of 5% [7]. It seems to affect most often smoking male patients, whose age is between 60 and 70 years old [8], as reported in our patient. The symptoms of laryngeal SCNEC are not specific, and depend essentially on the site of the tumor and its extent, with a predominance of involvement of the supraglottic region [9]. They include breathing and swallowing difficulties and hoarseness in different degrees. About half of all patients with laryngeal SCNEC have cervical lymph node metastases at presentation [10]. The diagnostic strategy is based on the one applied for squamous cell carcinomas of the larynx and it includes a medical history, clinical examination, panendoscopy with biopsy and neck, chest, abdominal CT scans [11].

The OctreoScan is a useful complement in the workup of NECs and is the most commonly used imaging modality in the diagnosis and workup of NECs. It sometimes detects lesions missed by CT or MRI [12]. In fact, Chiti et al. found that the OctreoScan was able to reveal abnormalities not previously detected on CT/MRI in about 28% of cases [13].

The diagnosis of this entity is based on the histopathological study combined with IHC. SCNECs are distinguished by cells with oval or spindle-shaped nuclei with dense chromatin without visible nucleoli and are small to medium size with poor cytoplasm [10]. A single positive endocrine marker such as synaptophysin, chromogranin or CD56 is considered sufficient for the diagnosis of SCNEC, according to the 2017 WHO classification of head and neck tumors [14].

Because of the rarity of this entity and the lack of randomized trials, there is no specific algorithm for the management of laryngeal SCNECs, however, it is mainly based on the one applied in lung SCNECs [15].

The treatment is multimodal, including chemotherapy, radiotherapy and surgery, combined or not, depending on the stage and extent of the disease [16]. The systemic treatment should be included in any therapeutic strategy due to the high dissemination potential of the disease, except for the small primary localized tumors without cervical lymph node involvement where surgery alone can be sufficient [9]. Chemotherapy can be indicated as neoadjuvant, concomitant or adjuvant treatment in non-metastatic state, in order to reduce the tumor volume and decrease the risk of distant metastasis [17].

The combination of chemotherapy and radiotherapy was the most used treatment for patients with localized or locally advanced disease. It achieved the best disease-specific survival at 5 years compared with other options (30.8% vs. 12.9%, P = 0.001) [18]. Our patient received neoadjuvant chemotherapy followed by concomitant chemoradiation. The doses of radiotherapy used are between 40 and 70 Gy when it is a definitive treatment; and between 50 and 60 Gy when it is an adjuvant treatment [9]. The addition of surgery to this combination in locally advanced laryngeal SCNECs did not show any benefit in terms of overall survival, which is in line with the results found in the pulmonary SCNECs, where the role of surgery remains very limited [17, 18].

The realization of a cranial prophylactic radiotherapy is controversial in extrapulmonary SCNC, because of the fact that brain metastases are less frequent compared to pulmonary SCNC [19].

Chemotherapy in the metastatic situation has proven to be effective in prolonging survival. The etoposide-cisplatin combination is the first-line treatment with a response rate of 69% [20].

CONCLUSION

In conclusion, laryngeal SCNCs are a rare and aggressive entity, with a high dissemination potential and a poor prognosis. The concomitant chemoradiation is the cornerstone of treatment of locally advanced disease while surgery doesn't seem to have an impact on overall survival. Even with a well-managed treatment, local and distant recurrences remain quite frequent.

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